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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,826	07/22/2003	Marcus E. Kehrli JR.	23015A	9210

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
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GROTON, CT 06340

EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,826	KEHRLI, MARCUS E.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-29 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1,3-10,13 and 15-29 is/are rejected.

7)☒ Claim(s) 2,11,12 and 14 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 22 July 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) 10 sheets
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1/16/04. 4 sheets
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-29 are pending in the present application.

2. Claims 3, 13, 18 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3 and 18 recite the limitation "the mammal" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claims 13 and 18 recite the limitation "the IL-18 protein" in line 1. There is insufficient antecedent basis for this limitation in the claim.

3. Claims 15-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are directed to methods for protecting a young mammal against an infectious disease comprising administering IL-18 to said mammal; the composition can also comprise other cytokines. The claims also recite that the infectious disease is caused by a protozoal, bacterial, fungal, or viral pathogen.

The specification discloses *in vitro* IFN-gamma production by isolated mononuclear cells (lymphocytes + monocytes) in response to mitogen stimulation (see figure 1). The specification (see pages 5-7) discloses an in vivo example of administering IL-18 to calves. The calves were still at less than 25% of adult capacity at 21 days of age. Calves that received 20 micrograms IL-18/kg, SC, 5X

had the highest observed levels of induced interferon-gamma production for a 5-day period beginning 3 days after the first injection (15.6% of adult capacity versus 7.9% for controls). This represents a nearly 100% increase relative to the average production of interferon-gamma by young control calves of the same age which had not been administered IL-18. For this 5-day period, the effect of increasing mononuclear cell interferon-gamma production was significant at $P<0.05$. Administration of recombinant bovine IL-18 at 20 micrograms/kg, SC, 5X, increased ex vivo interferon-gamma production by mitogen-stimulated mononuclear cells.

The specification is not enabled for methods for protecting a young mammal against an infectious disease comprising administering IL-18 to said mammal; the composition can also comprise other cytokines. The claims and the specification indicate that the infectious disease is caused by a protozoal, bacterial, fungal, or viral pathogen. However, the specification set forth no example of administering IL-18 to a young mammal and protection provided against infectious diseases. The state of the art at the time the invention was made indicates that *in vitro* experiments using macrophages stimulated IFN-gamma when incubated with IL-18. Shoda et al 1999 teaches that IL-18 is an immunoregulatory cytokine that may be pivotal in host defense against intracellular pathogens (abstract). Although IL-18 induces IFN gamma production *in vitro* and are important considerations for understanding mechanisms of protective immunity and designing vaccines for intracellular pathogens, Shoda et al teaches that the ability to analyze bovine IL-18 mRNA will be a valuable tool, and the development of reagents for bovine caspase-1 and IL-18 is still needed to understand the full significance of IL-18 in bovine immune responses (p. 1175, col. 2). Further, Musumeci et al teaches that

IL-18 maybe used in the treatment of patients with malaria, not that as a result of the administration of IL-18 the patient or mammal is protected against infectious diseases such as malaria. Neither the state of the art nor the present specification is enabled for methods for protecting a young mammal against an infectious disease (caused by a protozoal, bacterial, fungal, or viral pathogen) comprising administering IL-18 to said mammal. In view of the lack of teaching in the specification and the lack of information in the art available to one of skill in the art regarding the claimed method, there would be undue experimentation necessary for a person skilled in the art the practice the claimed invention of a methods for protecting a young mammal against an infectious disease (caused by a protozoal, bacterial, fungal, or viral pathogen) comprising administering IL-18 to said mammal.

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3-10 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicolson et al WO 99/56775 or Yamamoto et al RP 0845530. Nicolson et al, for example, discloses methods of administering IL-18, in a composition, to a mammal (abstract; examples; claims). Nicolson et al discloses that IL-18 is a cytokine that induces the production of IFN-gamma in established Th1 cells and that IL-18 use as a therapeutic and/or prophylactic agent in case of IFN-gamma susceptive diseases such as AIDS and certain cancers and tumors (pp. 1-2). Nicolson et al discloses that IL-18 can be obtained via extraction or

purification from natural sources, via organic chemical synthesis or via recombinant DNA technology (p. 3). Nicolson et al discloses the use of pharmaceutically acceptable carriers (p. 4) and that the mammal can be human or animal (p. 5). The claims of the prior art disclose that the IL-18 is of the same origin as the subject to be vaccinated (claim 5). The prior anticipates the claimed invention.

6. Claims 1, 3, 4, 7-10, 15, 16, 18, 19 and 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Fujioka et al 1999 (J. Virology, March 1999, 73/3:2401-2409).

Fujioka et al 1999 discloses a method of immunizing an animal (mouse) with a composition comprising IL-18 in a vehicle (i.e. pharmaceutically acceptable carrier) (abstract; materials and methods). The prior art discloses that the composition can also contain another cytokine such as IL-12 (materials and methods). The IL-18 that was used was made by recombinant means (materials and methods). Fujioka et al discloses that IL-18 protected against HSV type 1 infection and increased IFN-gamma production. The prior art discloses the claimed invention.

7. Claims 2, 11, 12 and 14 are objected to because they depend from a rejected claim.

8. No claims are allowed.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette R.F. Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. M. Minnifield
Primary Examiner
Art Unit 1645

NMM
September 23, 2004